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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,806	05/05/2005	Hashime Kanazawa	2005_0741A	8202

513 7590 05/31/2007

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EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
05/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,806	KANAZAWA ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 5/2005.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-24 are pending.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-9, 13-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite terms such as "anti-asthmatic'. "A drug" " " phosphodiesterase inhibitor"

It is unclear if applicant mean for them to be a method of "treating' or a "pharmaceutical compositions ".

The claims are being read as a method of treating and are being examined as such.

Applicants in their response should amend the claims to read "A method of ...."

Claim Rejections - 35 USC § 103

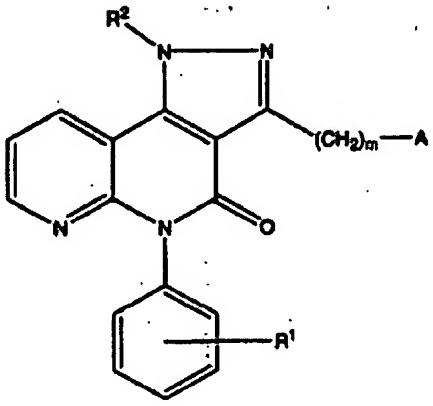
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0526,840 or US 5281610 Suzuki Fumio et al

Applicants claims are drawn to compounds , pharmaceutical compositions and methods of treating asthma.

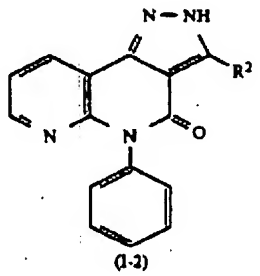
The compounds have the formula



wherein A is a phenyl or a pyridyl, an oxipyridyl or a thienyl and m is 1 to 4.

Determination of the scope and content of the prior art (MPEP §2141.01) .

The reference teaches compounds of the same core as given below.



(I-2)

wherein R2 is a alkyl, substituted or un substituted aryl, thienyl . These compounds also posses a bronch-dialatory effect.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The only different in the structure is the presence of (CH2)m linker in the instant claims.

The species in the application are drawn to m is 1, thus making the difference just a alkyl chain.

But the reference does teach just an alkyl group at the same position.Thus teaching that an alkyl or a ring such as a phenyl or a thienyl would be equivalent.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

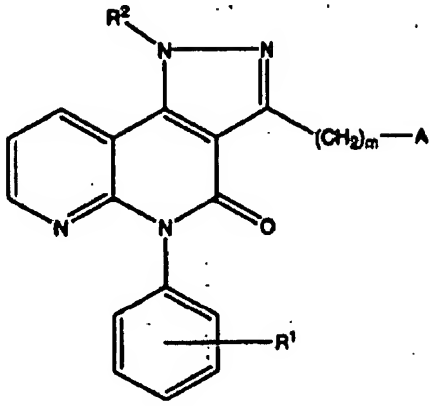
One of skill in the art in the business of making new drugs would have been motivated to make the minor change of having an alkyl linker to attach the phenyl or the thienyl group on the diazole ring. The close structural similarity would have motivated someone skilled in the art to modify the prior art by the addition of a CH2 to obtain the compounds af the invention and also expect them to retain its anti-asthmatic properties.

Claim Rejections - 35 USC § 103

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 06100561 Hashimoto Kinji et al in view of US 5281610 Suzuki Fumio et al

Applicants claims again are drawn to compounds , pharmaceutical compositions and methods of treating asthma. (immunomodulators and inflammation)

The compounds have the formula



wherein A is a phenyl or a pyridyl, an oxipyridyl or a thienyl and m is 1 to 4.

Determination of the scope and content of the prior art (MPEP §2141.01)

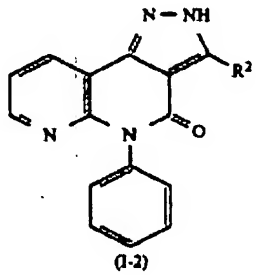
The JP'561 reference teaches several compounds in different tables. See table on page 47 which teaches the compounds wherein R8 is a benzyl and R1 is a substituted phenyl.

(Compound 100) .

These are used as immunomodulators.

Several compounds have been made with other substitutions on the carbon of the parazolo ring.

The US 5281610 teaches compounds of the same core as given below.



(I-2)

wherein R2 is a alkyl, substituted or un substituted aryl, thienyl . These compounds also possess a bronch-dialatory effect.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

In the prior art JP'561 the R8 is substituted on the N instead of the C of the pyrazolo ring.

However the teaching of the benzyl substitutent on the pyrazolo ring is there.

US '610 teaches the substitutent can be on the c of the pyrazolo ring.

Thus with the teaching of '610, one of skill in the art can modify the compounds of JP' 561 to make compounds which have a benzyl substitutent attached to the C atom instead of the N of the pyrazolo ring and expect the properties to remain the same.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some assay data and some asthamatic response , does not reasonably provide enablement for treating or the "propholaxis " of any condition related phosphodiesterase IV. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In applicant's arguments in paper #9, only two of the guidelines for making a determination of whether or not the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" have been used.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds of imidazo-naphthydrin core, its pharmaceutical compositions and method of treating.

2) The nature of the invention: The invention is a compound that is useful for prophylaxis and /or treat a disease or abnormal condition directly or indirectly related to phosphodiesterase IV (see claim 7). This includes a laundry list of diseases and disorders which can be treatable by inhibition of other receptor cites also.

3) The state of the prior art: There is very little known in the prophylaxis or treatment of any disease or abnormal condition directly or indirectly related to phosphodiesterase IV. The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the treatment or prophylaxis, as the in

vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art.

Also bioavailability plays a very important role in drug design and effects.

The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

Also compounds do not have an umbrella efficacy to treat a laundry list of disorders as implied by the specifications on pages 24 to 27.

The bioavailability of the compounds is different and that make the effect of a drug more unpredictable.

See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying

circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no examples that these compounds do in fact treat or have a prophylaxis effect for the above mentioned conditions. Each disease would have to be treated differently with different dose amount. There is no guidance in the specifications as to what the dose would be to treat a certain disorder. Page 32 has a general description of doses which can be in a 1000 fold range. The different diseases would have to be administered differently and applicants have not provided any guidance for the same.

7) The existence of working examples: The instant specification does not have any working examples. There is no data that these compounds do have a prophylaxis effect, nor is there any data that they do treat all the various disorders implied by the inhibition of phosphodiesterase IV.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome and almost impossible for one of skill in the art to find the right dose for each disease or condition, to see if does help in the prophylaxis and or treat the list of diseases. Experimentation with respect to treatment could be lethal if it doe not work and hence applicants should have provided more guidance.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that,

> based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Conclusion

Claims 1-24 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625

R.D.
May 25, 2007